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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/803,578	03/09/2001	Patrick Hwu	2026-4341	6841

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EXAMINER
LI, QIAN JANICE

ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
08/03/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/803,578	HWU ET AL.	
	Examiner	Art Unit	
	Q. Janice Li, M.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,7,8,10,40,41,44-46,52-61,71,72,74-76,79-87 and 89-93* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,7,8,10,40,41,44-46,52-61,71,72,74-76,79-87 and 89-93* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment, declaration of Dr. Patrick Hwu, and remarks submitted 6/8/2007 are acknowledged. Claims 72, 74, 81 have been amended.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 8, 40, 41, 45, 46, 52, 56, 58, 61, 71, 79, 80, 83, 86, 87, 92 stand rejected under 35 U.S.C. 102(b) as being anticipated by *Clay et al* (J Immunol 1999;163:507-13).

Clay et al teach a method for preparing tumor reactive lymphocytes comprising **a**). providing human peripheral blood lymphocytes (PBL) transduced with a recombinant retroviral vector encoding a chimeric receptor reactive to MART-1 tumor antigen and HLA-A2+ melanoma cells (e.g. the abstract, and page 508), wherein the receptor comprising α chain and β chain of a T cell receptor (e.g. fig. 1), and **b**). the transduced PBL cells were then co-cultured with irradiated allogeneic PBMC cells (comprising dendritic and B cells) and irradiated allogeneic EBV-B cells, whereby the cloids reactive to the allogeneic cells expanded (indicating the T cells contain an endogenous T-cell receptor reactive to the allogeneic cells). Thus, the co-culture mix contains the claimed T cell, allogeneic cell, and culture medium (a pharmaceutically acceptable carrier) Accordingly, *Clay et al* anticipate instant claims.

In the remarks, the applicant argues that the retroviral vector comprises the full-length alpha chain or the full-length beta chain of the TCR from MAER-reactive clone 5. As such Clay et al does not disclose a T lymphocyte comprising a recombinant chimeric receptor.

In response, it is noted the plain meaning of "chimeric" is "Composed of parts of different origin" (American Heritage Stedman's Medical Dictionary 2002). Since there is no structural limitation (e.g. full-length or fragment) for "chimeric receptor" in the claim, as long as the receptor is reactive with a tumor antigen, the receptor construct taught by *Clay et al* meets claim limitation because it is composed of at least two different parts, the alpha chain and the beta chain of a T cell receptor as shown in figure 1. Accordingly, *Clay et al* anticipate instant claims.

The prior rejection of Claims 1, 4, 7, 10, 40, 41, 44, 53-55, 57, 59, 60, 71-74, 79-85, 88, 89, 92, 93 under 35 U.S.C. 102(b) as being anticipated by *Hwu et al* (Cancer Res 1995;55:3369-73, IDS), is withdrawn in view of the declaration.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 4, 7, 8, 10, 40, 41, 44, 45, 46, 52-61, 71, 72, 74-76, 79-87, 89-93 are newly rejected under 35 U.S.C. 103(a) as being obvious over *Hwu et al* (Cancer Res 1995;55:3369-73, IDS), in view of *Munz et al* (J Immunol 1999;162:25-34, cited in the Office action mailed 3/28/06).

Hwu et al. teaches a method for preparing tumor reactive lymphocytes comprising **a**). providing murine tumor infiltrating lymphocytes (TIL) transduced with a recombinant retroviral vector (Mov-γ) encoding a chimeric receptor reactive with ovarian adenocarcinoma cells (e.g. the abstract, and column 2, page 3370), wherein the chimeric receptor comprising a single chain variable region from mAbs joined to the Fc receptor γ chain and capable of mediating T cell receptor signal transduction and binding FBP (e.g. column 2, page 3369), and **b**). the transduced TIL cells were co-cultured with syngeneic MC38 colon tumor cells, which results in a large amount of mIFN-γ production (indicating the TIL cells contain an endogenous T-cell receptor reactive with the syngeneic MC38 cells). Thus, the co-culture mix contains the claimed T cell, a syngeneic cell, and culture medium (a pharmaceutically acceptable carrier). The composition taught by *Hwu et al* differs from instantly claimed in that the tumor cell is syngenic, not allogenic.

Munz et al supplemented *Hwu et al* by establishing that using an allogenic cell as T cell stimulus is comparable to the syngenic/autologous stimulation in obtaining potent tumor reactive CTL cells. *Munz et al* co-cultured PBL with irradiated allogenic (T2 cells) or syngenic PBL (left column, page 26), and report the CTL obtained from allogenic APC allows the stimulation of high avidity cytotoxic T cell. *Munz et al* also teach the need in the art for the allorestricted T cells because the immune system of a cancer patient is often partially destroyed by chemotherapy or factors produced by tumor cells, and under such circumstance, allogenic APCs may be used for tumor antigen-specific T cell activation in immunosuppressed patients (e.g. the paragraph bridging pages 32-33), and concluded with respect to allogenic stimulated T lymphocytes, "SUCH T CELLS MIGHT INDEED BE USEFUL FOR TUMOR IMMUNOTHERAPY" (e.g. abstract).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the preparation process as taught by *Hwu et al,* with that of *Munz et al* by co-culturing either syngenic or allogenic APCs with T cells for activation, with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the claimed invention because the benefit as taught by *Munz et al.* Given numerous methods known in the art for T cell activation and expansion, this limitation falls within the bounds of optimization. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

Applicant's amendment of claims and disclosure necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is 571-272-0730. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on 571-272-0739. The **fax** numbers for the organization where this application or proceeding is assigned are **571-273-8300**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is **(866) 217-9197**. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at **800-786-9199**.

Q. JANICE LI, M.D.
PRIMARY EXAMINER

Q. Janice Li, M.D.
Primary Examiner
Art Unit 1633

QJL
July 23, 2007